Status of the claims

Claim 1 was amended to recite cells expressing a taste cell specific "GPCR." This amendment adds no new matter. Support for this amendment can be found, e.g., in the specification on page 32, lines 25-29.

Claim 6 was amended to recite an "increase or decrease" in binding. This amendment adds no new matter. Support for this amendment can be found, e.g., in the specification on page 13, lines 6-17.

Rejection under 35 U.S.C. § 112, second paragraph

"Binding"

Claims 1-4 and 6-8 were rejected as allegedly indefinite because the claims do not recite what type of binding will occur, e.g., an increase, a decrease, or no change in binding. Applicants respectfully traverse. The specification on page 13, lines 6-17 describe that determining the function effect refers to an assay that "increases or decreases" a parameter that is directly or indirectly under the influence of the claimed G-protein alpha subunit. The specification thus clearly describes the type of binding that will occur, e.g., an increase or a decrease. According to the MPEP § 2173.02, definiteness must be analyzed in light of: (A) the content of the application disclosure; (B) the teachings of the prior art, and (C) the claim interpretation that would be given by one of ordinary skill in the art. There is no requirement that the claim recite parameters that are defined in the specification and would clearly be understood by those of skill in the art, e.g., measurement of increased or decreased binding. However, to expedite prosecution, claim 6 has been amended to recite that an "increase or decrease" in radiolabeled GTP binding is measured. Applicants therefore respectfully request that the rejection be withdrawn.

Rejection under 35 U.S.C. §103

Claims 1-4 and 6-8 were rejected as allegedly unpatentable over Freissmuth in view of Wilkie. Freissmuth teaches a general method for identifying compounds that modulate

G proteins. Wilkie teaches amino acid sequence of SEQ ID NO:2. Applicants respectfully traverse.

As explained below, the Examiner has not established a prima facie case of obviousness. In order to establish a prima facie case of obviousness, the Examiner must demonstrate: (1) that the cited references teach or disclose all the claim elements; (2) that the prior art suggests that one of skill in the art modify or combine the reference teachings; and (3) that there is a reasonable expectation of success by one of skill in the art. MPEP § 2143.

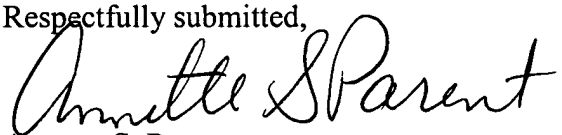
The cited references fail to teach or disclose all the claim elements. The present claims are directed to a method of identifying modulators of signal transduction in taste cells. None of the cited references teach or disclose that the claimed taste-specific G protein alpha subunit is co-expressed in a cell with a taste-specific G protein coupled receptor, therefore, one of skill in the art would not have been motivated to use this protein in the claimed cellular assays to identify modulators of taste cell activity. The claims have been amended to clarify that the assays of invention use cells in which the taste-specific G protein alpha subunit is co-expressed with a taste specific GPCR, and that the effect of the compound on the cell is used to select compounds that would modulate signaling in taste cells. Applicants therefore respectfully request that the rejection be withdrawn.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner has any questions regarding Applicant's response, or if the Examiner believes that a telephone conference would expedite consideration of this matter in any way, please call the undersigned at 415-576-0200.

Respectfully submitted,



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APPENDIX A

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION

Please amend the specification on page 4, lines 6-7:

The present invention demonstrates, for the first time, taste receptor cell specific expression of nucleic acids encoding G-protein alpha subunit. Specifically, the present invention identifies that Gα14, a G-protein alpha subunit, is specifically and selectively expressed in taste receptor cells. This gene was found to be co-expressed with G-protein coupled taste receptors, GPCR-B3 and GPCR-B4 (*see* USSN 09/361,652, filed July 27, 1999 and USSN 09/361,631, filed July 27, 1999, now US Patent 6,383,778). These taste receptors have been previously shown to be expressed in topographically distinct subpopulations of taste receptor cells and taste buds. These receptors are specifically localized to the taste pore, and are distantly related to putative mammalian pheromone receptors. The present invention thus demonstrates that Gα14 is specifically expressed in taste cells and further that it is co-expressed with GPCR-B3 and GPCR-B4 receptors in the different taste papillae. The G-protein alpha subunits that are specifically expressed in taste cells can thus be used, e.g., to screen for modulators of taste. The compounds identified by these assays would then be used by the food and pharmaceutical industries to customize taste, e.g., as additives to food or medicine so that the food or medicine tastes different to the subject who ingests it. For example, bitter medicines can be made to taste less bitter, and sweet substance can be enhanced.

Please amend the specification on page 11, lines 30-31:

"TC-GPCR" refers to a G-protein coupled receptor that is specifically expressed in taste receptor cells such as foliate, fungiform, and circumvallate cells. Such taste cells can be identified because they express molecules such as Gustducin, a taste cell specific G-protein (McLaughin *et al., Nature* 357:563-569 (1992)). Taste receptor cells can also be identified on the basis of morphology (*see, e.g.*, Roper, *supra*). Examples of TC-GPCR include GPCR-B3 and GPCR-B4 (*see, e.g.*, Hoon *et al., Cell* 96:541-551 (1999); *see also* USSN 09/361,652, filed July 27, 1999 and USSN 09/361,631, filed July 27, 1999, now US Patent 6,383,778), herein incorporated by reference in their entirety). TC-GPCRs encode G-protein coupled receptors with seven transmembrane regions that have "G-protein coupled receptor activity," as described below, e.g., they bind to G-proteins in response to extracellular stimuli and promote production of second messengers such as IP3, cAMP, and Ca2+ via stimulation of enzymes such as phospholipase C and adenylate cyclase (for a description of the structure and function of G-protein coupled receptors, *see, e.g.*, Fong, supra, and Baldwin, *supra*).

Please amend the specification on page 32, lines 26-27:

In a preferred embodiment, TC-Gα14 activity is measured by expressing TC-Gα14 in a heterologous cell with a TC-GPCR (*see* USSN 09/361,652, filed July 27, 1999 and USSN 09/361,631, filed July 27, 1999, now US Patent 6,383,778). As shown in Example I below, TC-Gα14 is specifically expressed in taste receptor cells, and also co-expressed with GPCR-B3 and GPCR-B4, in different taste papillae. As described above, HEK-293 cells may be used as a heterologous host cell, and modulation of taste transduction is assayed by measuring changes in intracellular Ca2+ levels.

Please amend the specification on page 59, lines 28-29:

These experiments demonstrate that $G\alpha_{14}$ is specifically and selectively expressed in circumvallate, foliate and fungiform taste receptor cells of the tongue, as shown

by *in situ* hybridization. Therefore, $G\alpha_{14}$ is a G alpha subunit that is specifically expressed in taste receptor cells. Furthermore, this gene is co-expressed with both GPCR-B3 and GPCR-B4 receptors in the different taste papillae (*see* USSN 09/361,652, filed July 27, 1999 and USSN. 09/361,631, filed July 27, 1999, now US Patent 6,383,778).

IN THE CLAIMS

1. (twice amended) A method for identifying a compound that modulates signal transduction in [sensory] taste cells, the method comprising the steps of:

(i) contacting [the compound with] a [sensory cell specific] cell which expresses a taste cell specific G-protein alpha subunit polypeptide and a taste cell specific G protein coupled receptor with the compound, the G-protein alpha subunit polypeptide comprising greater than 70% amino acid sequence identity to a polypeptide having a sequence of SEQ ID NO:2; and

(ii) determining a functional effect of the compound upon the cell expressing the G-protein alpha subunit polypeptide and the taste cell specific G protein coupled receptor, thereby identifying a compound that modulates signal transduction in [sensory] taste cells.

6. (once amended) The method of claim 1, wherein the functional effect is determined by measuring increased or decreased binding of radiolabeled GTP to the G-protein alpha subunit polypeptide or to a G protein comprising the G-protein alpha subunit polypeptide.